REMARKS

Entry of the above amendments and reconsideration and withdrawal of the rejection of claims 47 to 85 is respectfully requested. Claim 65 was cancelled without waiver or prejudice. Claims 47, 57, 66, 67, 68, and 84 were amended. Support for the amendments to Claim 47 may be found in the specification at page 3, lines 11-13; page 7, lines 16-20. Claims 57, 66, 67, and 68 were amended to change claim dependencies. Claim 84 was amended to reflect the amendments made in claim 47. Applicants reserve the right to file any subsequent application on cancelled subject matter.

1. Claims 47-84 and newly added claim 85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Petereit et al. (U.S. Pat. Appln. Pubn. No. 2002/0160042) in view of McAllister et al. (U.S. Pat. Appln. Pubn. No. 2003/0068369)

The Examiner states that Petereit teaches a process for producing moldings by injection-molding and injection-molded capsules made thereby, which comprise methacrylate copolymers composed of 50% to 70% by weight of methyl acrylate, 10 to 30% by weight of methyl methacrylate, and 5% to 15% by weight of methacrylic acid. The Examiner concedes that Petereit does not teach the instantly claimed amount of surfactant (of less than 2% as in claim 56); does not teach the instantly claimed amount of the lubricant stearyl alcohol (from about 10 to about 15%); does not teach absorption enhancers and does not teach a blend of hydroxypropyl cellulose polymers having a differing molecular weight. The Examiner states that McAllister ('369) teaches pharmaceutical polymeric compositions suitable for injection molding of single or multi-component pharmaceutical dosage forms comprising a plurality of drug substance containing sub-units, being capsule compartments and/or solid subunits comprising a sold matrix of a polymer which contains a drug substance, the sub-units being connected in the assembled dosage form by a weld between parts of the assembled dosage form. The Examiner alleges that "blends of hydroxypropyl cellulose polymers having differ molecular weight are disclosed at p. 12, ¶ 0150 and include KLUCEL. Suitable amounts of dissolution modifying agents (i.e., disintegrants) are about 10% to 40% as well as 10% to 70% for swellable solids such as hydroxypropylcellulose (p. 12, ¶ 0152). In the case where the claimed ranges 'overlap or lie inside ranges disclosed by the prior art' a prima facie case of obviousness exists." The Examiner alleges that it would have been obvious to one of ordinary skill in the art at the time the invention was made to include the specific

ranges/amounts of surfactant and lubricant, the absorption enhancers and blends of hydroxypropyl cellulose polymers as taught by McAllister ('369) within the formulations of Petereit.

Applicants respectfully traverse the rejection.

The USPTO provided guidelines regarding obviousness rejections following the decision of *KSR Int'l Co. v. Teleflex, Inc.*, No 04-1350 (U.S. Apr. 30, 1997):

> Obviousness is a question of law based on underlying factual inquiries. The factual inquiries enunciated by the Court [in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966)] are as follows:
>
> (1) Determining the scope and content of the prior art;
> (2) Ascertaining the differences between the claimed invention and the prior art; and
> (3) Resolving the level of ordinary skill in the pertinent art.
>
> Objective evidence relevant to the issue of obviousness must be evaluated by Office personnel. . . The question of obviousness must be resolved on the basis of these factual determinations. While each case is different and must be decided on its own facts, the *Graham* factors, including secondary considerations when present, are the controlling inquiries in any obviousness analysis. . .
>
> Once the *Graham* factual inquiries are resolved, Office personnel must determine whether the claimed invention would have been obvious to one of ordinary skill in the art. . .
>
> The key to supporting any rejection under 35 U.S.C. 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious. The Supreme Court in *KSR* noted that the analysis supporting a rejection under 35 U.S.C. 103 should be made explicit. The Court quoting *In re Kahn*, stated that "'[R]ejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.

Federal Register, Vol. 72, No. 195, 10/10/2007, pages 57526-575289.

To maintain objectivity, reference to MPEP 2141.01(a), Section I is warranted:

> The examiner must determine what is 'analogous prior art' for the purpose of analyzing the obviousness of the subject matter at issue. 'In order to rely on a reference as a basis for rejection of an applicant's invention, the reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the inventor was concerned.' *In re Oetiker*, 977 F.2d 1443, 1446, 24 USPQ2d 1443, 1445 (Fed. Cir. 1992)...
>
> A reference is reasonably pertinent if, even though it may be in a different field from that of the inventor's endeavor, it is one which, because of the matter with which it deals, logically would have commended itself to an inventor's

> attention in considering his problem. **Thus, the purposes of both the invention and the prior art are important in determining whether the reference is reasonably pertinent to the problem the invention attempts to solve.** If a reference disclosure has the same purpose as the claimed invention, the reference relates to the same problem, and that fact supports use of that reference in an obviousness rejection. An inventor may well have been motivated to consider the reference when making his invention. If it is directed to a different purpose, the inventor would accordingly have had less motivation or occasion to consider it.

MPEP 2141.01(a) at pages 1060-1061.

Applicants also direct attention to the MPEP states at 2143.01.IV:

> The prior art can be modified or combined to reject claims as *prima facie* obvious as long as there is a reasonable expectation of success. . . Obviousness does not require absolute predictability, however, **at least some degree of predictability is required**. Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness.

MPEP 2143.01 IV at pages 2100-2140.

The rejection is respectfully traversed for the reasons set forth in detail below.

First, nothing has been presented to show reasonable expectation of success when the prior art is combined. In light of the amendments to claim 47, Petereit would create technical problems for one skilled in the art. Particularly, one skilled in the art would be misled about the appropriate amount of Eudragit RL and/or RS used in the injection molding process. In the new proposed claims the amount of Eudragit RL and/or RS as stated in ingredient (i) starts from 20%. Petereit discloses in ¶ [0013] and [0014] that "another polymer" can be between 0 to 20%, where the amount is based on the (meth)acrylate copolymer a). Therefore, none of the Petereit mixtures can contain Eudragit RL and/or RS in at least 20% w/w of the entire mixture.

In fact, according to Petereit, the mixture containing the highest amount of ingredient g) (the "other polymer"), is when the mixture contains X grams of ingredient a) (the "methacrylate"), 0.1 parts of X of ingredient b) (the necessary "release agent") and 0 parts of all the remaining optional ingredients. Assuming X=100 grams, there will be 100 grams of a) plus 0.1 grams of b) and 20 grams of g), which will add up to 120.1 grams. In this mixture, g) is about 16.65% w/w. If other ingredients from c) to f) are present the amount of ingredient g) will necessarily

decrease. Hence, it would be impossible to read in Petereit a mixture containing more than 16.65% of ingredient g).

The Examiner also states that suitable amounts and/or ranges could be determined by one of ordinary skill in the art through routine or manipulative experimentation to obtain optimal results. Applicants respectfully disagree. Even "routine or manipulative experimentation" would not teach or suggest Applicants' ranges for the amounts in Eudragit RL and/or RS. Instead one skilled in the art would need to make notable changes in the basic ratios taught by Petereit. In addition, Petereit teaches away from using the 20 to about 50% w/w range for Eudragit RL and/or RS disclosed in Applicants' application. One skilled in the art would need to work outside the scope that Petereit suggested.

Second, in light an additional amendment to claim 47, ingredient ii) must now have at least one dissolution modifying excipient present in a certain range and a blend of HPCs of different molecular weights. The Examiner states that she has read blends of HPC in ¶ 150 of McAllister '369 (and a corresponding paragraph of McAllister '311):

> [0150] More specifically, the class of agents known as swellable solids for use as dissolution modifying agents, includes but is not limited to poly(ethylene)oxide, the cellulosic derivatives, such as ethyl cellulose and cellulose acetate phthalate; hydroxypropylcellulose (HPC), especially at lower molecular weights, e.g., KLUCEL EF and LF grades, available from Aqualon, hydroxypropylmethyl cellulose, and other hydroxyalkylcellulose derivatives. Suitably, the swellable solids used as dissolution modifying excipients are in the range of about 5% to about 70% w/w, preferably about 10 to 50%. Dependent upon whether an immediate or a longer dissolution rate profile is indicated, the amount of HPC, if so used, will vary. If an immediate dissolution rate is preferred than preferably there is about 40 to 70% w/w HPC present. If a modified pulse release rate profile is preferred, than the amount of HPC will be decreased, and suitably additional dissolution modifying excipients in combination with HPC will be used. Therefore the amount of HPC may vary from about 5 to 70% w/w. In combination, HPC is likely to present from 10 to 40% w/w, preferably <30% w/w.

Applicants respectfully disagree. It appears that McAllister '369 as well as McAllister '311 does not mention HPC blends of different molecular weights. At best, these two prior art references mention HPC grades of different molecular weight where Klucel EF and JF are mentioned. Applicants submit that the Examiner has read more that what is indicated or suggested in McAllister '369 and McAllister '311. No blends of HPC are either disclosed or exemplified.

Such a HPC blend is crucial to the present invention. As demonstrated in Examples 4 and 5 in the present application, where both examples use the same composition, ingredients, amount of ingredients, the technical effect of just using a blend of HPC grades of different molecular weight in one and not the other resulted in visible differences in shell structure and in the molding process:

Example 4 ¶ [0103]: Additional Shell observations: Good mouldings, very little cracking.
¶ [0104]: variable release times from 58 to 100 minutes

Example 5 ¶ [0110]: Very good mouldings, shells are completely clear, no cracking on welding
¶ [0111]: very reproducible detachment ranging betw 36-40 minutes for 65 samples.

From a structural and dissolution standpoint, the use of a blend of HPC grades of different molecular weight has improved the performance of an identical composition using a single HPC grade. Since neither McAllister '369 nor Petereit explicitly or implicitly teaches a HPC blend of different molecular weight or the amount of Eudragit RL and/or RS, Applicants submit that the prior art has failed to disclose all elements of the invention, rendering Applicants' invention patently distinct from the cited references.

Based on the arguments above, Applicants respectfully request that the Examiner reconsider and withdraw the 35 U.S.C. § 103(a) rejection of claims 47 to 85.

2. Claims 44-64, 69-77, 82 and 83 are rejected under 35 U.S.C. 103(a) as being unpatentable over Petereit et al (U.S. Pat. Appln. Pubn. No. 2002/0160042) in view of McAllister et al. (U.S. Pat. Appln. Pubn. No. 2003/0049311).

The Examiner states that Petereit teaches a process for producing moldings by injection-molding and injection-molded capsules made thereby, which comprise methacrylate copolymers composed of 50% to 70% by weight of methyl acrylate, 10 to 30% by weight of methyl methacrylate, and 5% to 15% by weight of methacrylic acid. The Examiner concedes that Petereit does not teach the instantly claimed amount of surfactant (of less than 2% as in claim 56); does not teach the instantly claimed amount of the lubricant stearyl alcohol (from about 10 to about 15%); does not teach absorption enhancers and does not teach a blend of hydroxypropyl cellulose polymers having a differing molecular weight. The Examiner states that McAllister ('311) teaches pharmaceutical polymeric compositions suitable for injection molding of single or multi-component pharmaceutical dosage forms comprising a plurality of drug substance containing sub-units, being capsule compartments and/or solid subunits comprising a solid

matrix of a polymer which contains a drug substance, the sub-units being connected in the assembled dosage form by a weld between parts of the assembled dosage form. The Examiner states that the "dissolution modifying agents can comprise hydroxypropylmethyl cellulose and other hydroxyalkyl cellulose derivatives p. 11, ¶ 0146-0147. Suitable amounts of dissolution modifying agents (i.e. disintegrants, swellable solids) are from 2.5% to 70% w/w (p. 11, ¶ 0146). In this case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. In re Woodruff, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990)." The Examiner alleges that it would have been obvious to one of ordinary skill in the art at the time the invention was made to include the specific ranges/amounts of surfactant and lubricant, the absorption enhancers and blends of hydroxypropyl cellulose polymers as taught by McAllister ('311) within the formulations of Petereit.

Applicants respectfully traverse the rejection. As noted above nowhere in ¶ [0146-0147] is a HPC blend mentioned. Applicants that the rejection is moot in light of the amendments to claim 47.

Based on the arguments above, Applicants respectfully request that the Examiner reconsider and withdraw the 35 U.S.C. § 103(a) rejection of claims 44-64, 69-77, 82 and 83.

CONCLUSION

Applicant respectfully requests reconsideration of the rejection of the above-mentioned claims and request an early and favorable allowance.

Respectfully submitted,

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